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ON ARRESTED DEVELOPMENT AND LITTLE'S DISEASE.[1]

By WILLIAM G. SPILLER, M.D.,

With Remarks by W. W. Keen, M.D., On the Advisability of Operation in Microcephaly.

The diagnosis of arrested development is so frequently made that the desire naturally arises to know the facts obtained by actual examination of brain and cord in such cases, and in this paper an attempt is made to present a few of these, especially those relating to arrested development of the motor tracts. The clinical notes have in great part been taken from the casebook of Prof. Keen, at the Philadelphia Orthopedic Hospital and Infirmary for Nervous Diseases. I am deeply indebted to him for the liberality he has manifested in placing them at my disposal. Use has also been made of the paper published by Prof. Keen in the American Journal of the Medical Sciences, June, 1891. The case K. K. is from the Pennsylvania Training School for Feeble Minded Children.

The parents of the child K. K. were first cousins, and of moderate intelligence. One child, still living, has hydrocephalus; another died in his fourth month in convulsions.

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[1] From the Wistar Institute of Anatomy and Biology. One of two papers presented for membership in the American Neurological Association.

K. K. had a very small head at birth, and the anterior fontanelle was closed. She was born in difficult labor, at full term, without the use of instruments, and was the second child in the family. The mother fell down ten steps and hurt her side in the seventh month of pregnancy. No history of venereal disease in the parents could be obtained. At the age of nineteen months, K. K. was unable to sit erect without support, though she could hold objects in her hands. She had moderate contracture of the flexor muscles of the feet, but her legs were not paralyzed. The knee-jerks were absent, possibly on account of contracture, and ankle-clonus was not observed. The child presented the appearance of an idiot, and her attention could only be obtained momentarily. Convulsions occurred in the teething period. The measurements at the age of nineteen months were as follows:

Biparietal	10.3 cm.	(4 1-16 in.)
Biauricular	10.2 cm.	
Bitemporal	8.3 cm.	(3 1-2 in.)
Occipito-frontal	11.9 cm.	(4 3-4 in.)
Circumference	36 cm.	(14 1-4 in.)

By comparison with average measurements it will be seen that the head was not much larger than that of a fetus at full term. Craniotomy was performed when the patient was nineteen months old. The description by Dr. Keen of the operation is as follows: "An incision was made one inch to the left of the middle line, parallel to the sagittal suture, and six inches in length. A curved incision was then made from the anterior end of this line downward, so as to lift a frontal flap, the scar of which would be hidden by the hair. A half-inch button of bone was removed by the trephine, and from this anteriorly and posteriorly a furrow, a quarter of an inch wide, was cut out of the bone, extending to within an inch of the supraorbital ridge and an inch above and to the left of the inion. The length of the furrow was five inches. The amount of hemorrhage from the scalp was very slight, much less than I have found in adults. The bone was very thin, about one to one and a-half mm. thick only, but bled freely. Opposite the parietal boss the dura was very adherent to the bone, but at all other points was separated easily. When the point of a pair of scissors was put under the flap of bone thus loosened, and the handle of the scissors let down gently, the simple weight lifted the flap perceptibly. The periosteum corresponding to the bone removed was cut away. The dura had not been opened, and appeared normal. A few strands of horsehair were placed in the furrow, and the wound dressed. The operation lasted half an hour. The temperature at its close was 98 deg."

Three months later a linear craniotomy was performed in precisely the same manner on the other side of the head.

The condition of the child was thought to be improved to some slight degree after the operation, though this improvement may have been due to the attention she received at the Children's Hospital from the chief nurse, Miss Hogan. When two and a half years old, K. K. could only say "Mammy." The arms and legs were freely moved, but incoördinately, and motion was greater in the former. She could sit up without support, but if placed upon her feet she fell at once to the floor. Her intelligence was of very low grade.

In Dr. Llewellyn's report of her condition during her residence at the Pennsylvania Training School for Feeble-Minded Children, and just before her death, the statements are made that K. K. could not stand; could not feed herself, and had little use of her hands, though she could understand many things said to her.

She died suddenly at the age of six. When seen after death the feet were in the position of marked talipes equino-varus, and the toes were flexed. The thenar and hypothenar eminences of the hands were of nearly normal development; the thumbs were not flexed; the first phalanges of all the fingers were extended, and the second and third moderately flexed. Her form was very slight. The circumference of the head through the glabella and inion was sixteen inches. In removing the calvarium the dura was found to be very adherent near and along the sagittal suture. The brain was small, and weighed sixteen ounces avoirdupois. The pia was not adherent. There were no abnormal depressions, and no sclerotic areas, and the gyri and fissures were well developed. There was not the slightest indication of microgyria. The cord was very small.

From the clinical description, which has been confirmed by several, as the child was studied by a number of physicians, the affection was not unlike the disease described by Little, which in France and Germany is more frequently called by his name than in England. The labor was difficult, but neither this nor premature birth was the cause of the child's condition. The definition which Brissaud[2] gives of Little's disease, which is in reality merely a symptom-complex, is as follows: "Spastic and congenital paraplegia of the four limbs, more pronounced in the inferior, occurring especially in children born before full term, characterized by spasm more than by paralysis, and not associated with convulsions or disturbance of intellect, and capable of progressive amelioration, if not of complete cure." Little,[3] however, spoke of impairment of the intellect. Freud[4] says there are cases of diplegia in which premature birth and difficult labor are not the causes of the paralysis, but that there is a predisposition to paralysis in these children which, if sufficiently strong, may develop into diplegia, without the occurrence of trauma. The majority of children born before full term, or in a condition of asphyxia resulting from dystocia, do not present diplegia. This case of K. K. is of unusual interest, for Marie[5] states that there has as yet been no autopsy in a case of Little's disease.[6] He thinks dystocia or disease of the mother or fetus in certain cases may possibly produce spastic dorsal tabes (Little's disease) in children born at term, but the most common cause is premature birth, and the condition is one of imperfect development of the pyramidal fibres, as is seen in the case K. K. Emphasis must be laid on the statement that *there was no macroscopic lesion* in my case. It is impossible to state the degree of spasticity which was manifested by the child K. K., inasmuch as I never saw her in life, but the contractures of the flexor muscles of the feet at the age of nineteen months and after death indicate that the muscular tonus was exaggerated. The child also was not paralyzed. To those who object to the title of Little's disease for this case on account of the birth at full term, the presence of microcephaly, and the insufficient degree of spasticity, the name of cerebral diplegia in the sense used by Freud,[7] or of "infantile spastic state of cerebral origin *(états spasmodiques infantiles d'origine cérébrale)* suggested by Van Gehuchten,[8] may be more acceptable.

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[2] Brissaud: Maladies Nerveuses, p. 110.

[3] Little: Transactions of the Obstetrical Society of London, vol. iii., pp. 306, 307.

[4] Freud: Revue Neurologique, 1893, p. 183.

[5] Marie: Traité de Médecine, vol. vi., p. 457.

Sections from the superior part of the ascending frontal convolution of the right and left sides of the brain of K. K., in the portions which contain the centres for the lower extremities, and especially from the paracentral lobule, show an absence of the very large ganglion cells, *(Riesenzellen)*, which are found in a normal motor cortex. The cells of the third layer (Cajal) are a little larger than those of the second, and some are of very good size; but there is great diminution of the giant cells which are present in sections from a normal brain of a child of about the same age, taken from the same portions of the cortex for comparison. It may, however, be possible to find one or two cells of unusual size in a field, but they are always much smaller than the largest of the giant cells of a normal cortex. The condition can hardly be attributed to the age of the child. Some of the few cells present in the anterior horns of the cord are large. The pyramidal cells of Betz[9] are said to be the largest cells in the entire nervous system, excepting some in the spinal ganglia, and are found in the motor cortex. They resemble the cells of the spinal cord. Betz stated that they are found chiefly in the fourth of his five cortical layers; that they are less numerous in the lower half of the anterior central gyrus, and are most abundant in the paracentral lobule. He has found them in the brain of idiots *(Riesenpyramiden, Nervenriesenzellen)*. V. Monakow[10] cut the fibres of the inner capsule of a cat. The histological examination of the motor cortex was most astonishing, according to his statements. Betz's giant cells had entirely disappeared, while the other layers presented no noteworthy changes. Mahaim[11] says that the connection of the giant cells with the pyramidal fibres has also been demonstrated by v. Gudden and Moeli in the rabbit and guinea pig, and by Moeli and Henschen in man.

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[6] The cases of Dejerine reported to the Société de Biologie were published after this paper was written.

[7] Freud: Zur Kenntniss der cerebralen Diplegien des Kindesalters.

[8] Van Gehuchten: Revue Neurologique, Feb 15, 1897.

The apical processes of the pyramidal cells in the cerebral cortex of K. K. point toward the surface, and do not cross one another in the irregular arrangement described by some writers. The anterior pyramids of the oblongata are small, but present no evidences of degeneration. It has not been possible to obtain an oblongata or cord from a child of exactly the same age for comparison, but the whole central nervous system is much smaller than that from another child of seven years. There are very few cells in the anterior horns of the cervical swelling, though those which are present have a normal appearance. The horns are small. The crossed pyramidal tracts and columns of Goll are decidedly less intensely stained by the method of Weigert. In carmin sections an increase of the neuroglia is very evident in the columns of Goll, and while the fibres of the anterior and lateral columns are small, those in the crossed pyramidal tracts are of unusually fine calibre, and are smaller than those in Goll's columns. The thoracic portion of the cord is very small. The anterior horns of the lumbar region contain a few cells of normal appearance. The anterior and posterior spinal roots are normal. Serial sections have been made of the central nervous system from the oblongata into the thalamic region, but they have not revealed anything further worthy of special note. This case K. K. seems to be similar to the one described by Mya and Levi (quoted by Van Gehuchten). Their patient was born in difficult labor at full term, was of feeble intellect, and presented general muscular rigidity. Partial agenesia of the pyramidal tracts in the cord, and incomplete development of the pyramidal cells of the motor cortex were found.

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[9] Betz: Centralblatt für die medicinischen Wissenschaften, 1874 and 1881.

[10] V. Monakow: Neurologisches Centralblatt, 1883.

[11] Mahaim: Archiv für Psychiatrie, xxv.

Ganghofner[12] has reported a case of what was apparently general spasticity. Sections from the upper part of one anterior central gyrus appeared normal, but a scarcity of fibres in the crossed pyramidal tracts of the cord was noticed. Macroscopically the brain and cord were normal, and yet he believes that the cortex could not really have been perfectly developed. In two other cases of spasticity in which no peculiar findings were observed by the microscope he thinks there may have been a moderate decrease of the pyramidal fibres which eluded detection.

Otto[13] has reported two cases of idiocy. One of his patients was unable to walk or stand, but could move the limbs feebly while in bed. He could neither speak nor understand anything said to him. The other child presented contractures in all the extremities. Microgyria was found in both cases at the autopsy, and in the microscopical investigation decided anomalies were observed in the cellular elements, although the fibres of the cerebral cortex presented no great variation from the normal. The cells were quite numerous, well developed, and regularly placed in the layer of small pyramidal cells. The large pyramidal cells were almost entirely absent, and those that were present were little larger than the small pyramidal cells. There were no giant pyramidal cells at all in the frontal and central lobes, but there were many round ganglion cells. In his cases the pyramidal tracts in the oblongata contained fewer fibres than normal, but they were not degenerated, and this deficiency of fibres he attributes to the scarcity of cortical ganglion cells. The ganglion cells of the cord, contrary to the condition in my case, were well developed. In Anton's case the pyramidal tracts were very small, and the central gyri were affected as in Otto's case (Otto). Otto states that these giant cells of the cerebral cortex are developed in normal brains at the time of birth. He found also pale gray areas in the white matter of the hemispheres which were formed by collections of ganglion cells between the fibres of the white matter. They were evidently nerve cells, for many were pyramidal in shape and had processes.

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[12] Ganghofner: Zeitschrift für Heilkunde, vol. xvii., 1896.

[13] Otto: Arvhiv für Psychiatrie, vol. xxiii., p. 153.

Binswanger[14] also has reported a case of microgyria. The child was unable to stand, walk, speak, or understand what was said to him. The limbs were contractured. The central gyri in both hemispheres were absent. In sections from the left frontal lobe near the defect the giant cells (*Riesenzellen* of Betz), were absent. There was no secondary degeneration of the pyramidal tracts of the cord, and the cells of the anterior horns showed no pathological changes. The fibres in the white matter of the cord were possibly a little smaller. The anterior horns, especially in the lower part of the cord, were relatively small, and the cells seemed to be less numerous.

In the case of idiocy with microcephaly, reported by Popoff,[15] the cortical nerve cells were unequally distributed, and in some places had an irregular arrangement. The apical processes of the pyramidal cells in normal brains are parallel to one another; but in Popoff's case, they crossed at an acute angle. In some portions there was a decrease in the number of nerve cells, and most of the cells were small and occasionally their contour was abnormal. The cortical vessels were more or less thickened. In the frontal and paracentral lobes the giant cells were quite hard to find, and had not attained a large size. The left cerebral hemisphere was more flattened and smaller in its anterior portion than the right. During life the right upper limb was adducted, and the forearm, hand and fingers were flexed.

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[14] Binswanger: Virchow's Archiv, 1882, p. 427.

[15] Popoff: Archiv für Psychiatrie, xxv., 1893.

Köster[16] in the brain of an idiot found thickening of the neuroglia, enlargement of the pericellular and perivascular spaces, decrease in nerve cells in certain parts, and, in some, deposits of pigment. In some shrivelled cells there was no nucleus. He also found the irregular arrangement of the pyramidal cells. Some of these were parallel to the surface of the cortex, lying on their side. Köster gives a brief review of some of the earlier investigations on idiotic brains.

Oppenheim[17] observed an increased number of the small round cells of the cortex in microgyria; the pyramidal cells in places were entirely absent, or imperfectly formed and abnormally placed.

Friedmann[18] describes a case of infantile spastic paraplegia associated with idiocy. One hand was contractured. The brain and spinal cord, with the exception of the posterior columns, were smaller than normal. The pyramidal cells of the cortex were reduced to about half the usual number, the pericellular spaces were enlarged, the small vessels were distended, and their walls had undergone hyaline degeneration. The number of the vessels was less than normal. Some of the cortical pyramidal cells were altered in shape. Diffuse areas of sclerosis were found all through both hemispheres. The mass of white matter was greatly diminished. The pyramidal tracts and all the white columns of the cord, except the posterior, were small. Friedmann is inclined to attribute the condition in this case primarily to the changes in the small vessels.

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[16] Köster: Neurologisches Centralblatt, 1889, No. 10.

[17] Oppenheim: Neurologisches Centralblatt, 1895, p. 131.

[18] Friedmann: Deutsche Zeitschrift für Nervenheilkunde, vol. iii.

B. Sachs[19] has reported a case which is not so well known in the foreign literature as it deserves to be. He claims that it is the first case of congenital spastic paraplegia examined microscopically. In this case the labor was difficult, and the child was asphyxiated when born. Convulsions were frequent in early infancy. Convergent strabismus was present. The deep reflexes were increased. The mental development was deficient, but the child was not absolutely idiotic. It was one year old at the time of death. Sachs found thickening of the pia, characterized by general cellular infiltration; its blood vessels showed marked cellular proliferation, and the pia was adherent to the cortex. In the cortex itself there were few, if any, normal pyramidal cells. In the outer layers, and particularly in what would correspond to Meynert's third and fourth layers, there was an enormous profusion of small glia cells. The blood vessels were in part normal, but many of them showed marked small cell proliferation of the walls. There was unquestionably a thickening of the neuroglia. The anatomical diagnosis was chronic meningo-encephalitis. Sachs considered the case to be due to a wide-spread effusion of blood between the pia and the cortex at the time of birth. The spinal cord revealed a most distinct degeneration of both lateral columns, secondary to the cortical lesion. This degeneration could be recognized in all parts of the motor tracts. There is no degeneration of the lateral tracts in the case K. K., but the condition is one of partial agenesia.

In his work on the nervous diseases of children,

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[19] Sachs: New York Medical Journal, 1891, vol. i.

Sachs[20] speaks again of this case and states that the upper extremities were less paralyzed, but somewhat rigid. What at first he supposed to be secondary degeneration of the pyramidal tracts he later concluded was a primary and congenital defect. In another case of arrested cerebral development published by him,[21] the cortical ganglion cells were very imperfectly formed, and were not numerous. There was no trace of a previous encephalitic process, and no change in the blood vessels. He speaks again of this case in his paper on amaurotic family idiocy.[22] In the brain from the sister of this patient similar findings were observed, and in the lower part of the cord (the upper portion was lost), the lateral columns presented a degeneration that "was very different in character and extent from an ordinary secondary degeneration." Sachs regarded the condition of the pyramidal cells of the cortex as a sign of arrested development and not of inflammation. Kingdon[23] also noted changes in the cortical pyramidal cells in his case of amaurotic family idiocy, as well as "well-marked descending degeneration" in the cervical region of the cord.

Schiff[24] found that after removal of the sigmoid gyrus in a dog twelve days old, the pyramidal tract of the opposite side in the cervical region stained more deeply with the carmine than normally, when examined seventeen weeks after the operation. On the same side of the cord there was a small red patch in the pyramidal tract. He was much surprised to find that there was no true secondary degeneration, but instead of this the pyramidal tracts were filled with thin nerve fibres with very small axis cylinders. He later observed this diminution in the size of the pyramidal fibres in six cases, and in all these the area occupied by the small fibres was not the same. In none of these cases did he find any true degeneration, even when the animal had lived five months after the operation. In one case the greater part of both lateral columns was involved, and in another small fibres were found in nearly all the white columns. Schiff says it might be imagined that true secondary degeneration in young animals does not occur. This idea is incorrect, for Löwenthal[25] has shown that this may be found in a kitten fourteen days after section of the posterior part of the lateral column. Schiff has obtained this result also in young dogs. However, six cases prove the frequency of simple atrophy of motor fibres after a cortical lesion in early life. These fine fibres are present in the case K. K., but we must not forget that in a child the nerve fibres are smaller than in an adult, and do not attain their full development for a long time, as Hösel[26] has stated. Still, making allowance for this fact, there is no doubt that the pyramidal fibres are of uniformly finer calibre than those of any other part of the cord, and *much* smaller than in the child of seven years. They probably represent a condition of agenesia.

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[20] Sachs: Nervous Diseases of Children, p. 399.

[21] Sachs: Journal of Nervous and Mental Disease, 1887.

[22] Sachs: New York Medical Journal, May 30, 1896.

[23] Kingdon: Transactions of the Ophthalmological Society of the United Kingdom, vol. xii., 1892.

[24] Schiff: Centralblatt für Physiologie, 1893, p. 7.

It will be noticed in Otto's case (l. c.) that there was no degeneration of the fibres of the pyramidal tracts, but merely a diminution in the number of fibres. It cannot be said that there is a diminution in the number of fibres in the case K. K. They are very small and, therefore, many are crowded together in a given area. Oppenheim[27] has reported atrophy of the direct and crossed pyramidal tract from porencephaly. There was no true degeneration, although a slight increase of neuroglia, and possibly a degeneration of scattered fibres. There are many similar cases in the literature. Gierlich[28] examined a case in which the motor tract had been affected within the internal capsule very early in childhood. The pyramidal tract was smaller, but the fibres were not of diminished calibre, although their number was less than in the corresponding tract of the opposite side. There were no evidences of degeneration. His explanation for the paucity of nerve fibres and absence of sclerosis is that either a downward growth of motor fibres from the cortex did not take place, or else reactive inflammation did not develop after destruction and absorption of the young fibres. Hervouet[29] also thought that there was a deficiency of development of the nerve fibres of the lateral columns, without sclerosis, in his case of idiocy. In Popoff's[30] case of idiocy the gyri of both hemispheres were thin, but the left hemisphere was smaller than the right in its anterior part. The lateral column and horns of the right side of the cord were smaller than normal, and above the motor decussation the left pyramidal tract was small. This diminution in size of the right horns and lateral column was due to imperfect development, for there was no sclerosis, and the nerve fibres had probably never developed as in a normal cord. It has been known for a long time that micromyelia may be associated with microcephaly (Aeby, Thiele, Flesch, Schattenberg: quoted by Popoff).

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[25] Löwenthal: Recueil zoolog. Suisse, vol. iv., p. 111, quoted by Schiff.

[26] Hösel: Archiv für Psychiatrie, vol. xxiv., p. 480.

[27] Oppenheim: Neurologisches Centralblatt, 1895, p. 132.

[28] Gierlich: Archiv für Psychiatrie, vol. xxiii.

Anton[31] has reported four cases of fetal or early cerebral disease which caused deficient development of the pyramidal tracts. In one of his cases there was absence of the pyramidal tracts, and yet the gray matter of the cord was well developed. He believed that in complete agenesia of these tracts the spinal gray matter suffers very little or not at all, and states that no writer has reported changes in the anterior horns in micromyelia. This view is not tenable. In Popoff's case the right anterior horn in the cord was much smaller and there were proportionally fewer cells within it, although the cells present were neither sclerosed nor atrophied. One side of the cord, including the anterior horn, was smaller also in Hervouet's case (l. c.), although the cells of the anterior horns were normal. In this case the columns of Goll presented the appearance of ascending degeneration, as in my case, and yet there was no lesion to be detected which could have caused an ascending degeneration. Hervouet regarded this condition of the cord as one of arrested development. The case K. K. also is contrary to Anton's view. The anterior horns of the cervical swelling are under-size and contain very few nerve cells. In Muratoff's[32] case of bilateral porencephaly there were atrophied cells in the anterior horns of the cervical cord, and in the thoracic and lumbar portions scattered atrophic cells were found. The pyramidal tracts were degenerated, and this probably explains the condition of the ganglion cells of the cord. An abnormal condition of these cells probably frequently occurs when the pyramidal fibres are imperfectly developed in the child. In Muratoff's case No. VI., (an idiotic, microcephalic child), there was imperfect development of the pyramidal fibres, total atrophy of the cortical cells of the central lobe, and absence of the tangential fibres. The motor cells of the anterior horns of the cord were atrophied; the cellular processes were indistinct; and the cells though small were present in normal numbers. Railton,[33] in a case of double spastic hemiplegia, found the pyramidal tracts normal, and in the motor area (cortex?) there was a diminution in the number of the large ganglion cells and some increase in neuroglia. Marchand[34] says the nervous elements are in normal arrangement, though lessened in number, in uncomplicated cases of microcephaly.

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[29] Hervouet: Archives de Physiologie, 1884.

[30] Popoff: Archiv für Psychiatrie, vol. xxv.

[31] Anton: Ueber angeborene Erkrankungen des Centralnervensystems, 1890, quoted by Popoff.

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[32] Muratoff: Deutsche Zeitschrift für Nervenheilkunde, vol. vii.

[33] Railton: British Medical Journal, 1892, vol. i., p. 441.

[34] Marchand: Abstract in Centralblatt für allgemeine Pathologie und pathologische Anatomie, 1892, p. 780.

Steinlechner-Gretschischnikoff[35] in two cases of microcephaly observed imperfect development of the cord, chiefly in the pyramidal tracts, anterior columns and columns of Goll, and, in one case, in the direct pyramidal tracts. In one of these cases there were fewer ganglion cells in the gray matter of the cord. The statement by this authoress that the normal development of the columns of Goll, as well as of the pyramidal tracts, is dependent upon the development of the cerebrum, is in accordance with the findings in the case K. K. The experiments of Ceni[36] (of Milan) in hemisection of the posterior columns with the remarkable resulting changes in the cortical cells of the sigmoid gyrus and occipital lobe, chiefly of the side opposite to the hemisection, as seen by the silver method, would seem to show a connection between the fibres of the posterior columns and the cortical cells. The number of the cells in the anterior horns in microcephaly is usually less than in normal cords, according to Steinlechner-Gretschischnikoff.

Van Gehuchten[37] has found that the pyramidal fibres, even the axis cylinders, are entirely absent in the cord of a normal fetus of seven months, but are present in and above the anterior pyramids. Spastic rigidity in children born before full term, according to him, is not due to the absence of the myelin sheaths, nor to deficiency of the pyramidal tracts in their entire length, but to an arrest of the downward growth of these fibres. Flechsig claimed that the pyramidal tracts develop from above downward, and Starr[38] has offered a forcible argument in favor of this view from the study of a most extraordinary case of microcephaly in which the cerebral hemispheres were absent, and the pyramidal tracts had not developed.

Hervouet (l. c.) has shown that the pyramidal tracts are not fully developed until about the fourth year of extrauterine life. Perhaps here is the explanation of the fact that the tendency to bilateral cerebral paralysis seems to cease in early childhood. The extrauterine cerebral paralysis in childhood is usually unilateral (Higier).[39] Sachs[40] has seen no case of cerebral diplegia or paraplegia which had begun after the fourth year, and he says that the tendency to bilateral cerebral affections seems to cease early in life. If the pyramidal fibres are so imperfectly formed in the first few years of the extrauterine period, they are more exposed to injury, and especially in their distal ends. It is not impossible that the degeneration seen in combined systemic disease, as for example in Strümpell's[41] case or in many others, may be explained by the direction of the growth of the fibres. The sensory fibres grow upward in the cord, in the same way that the motor fibres develop downward. In combined systemic disease the pyramidal tract is usually most degenerated in the lower regions of the cord, and the posterior columns in the upper portion, i. e., in the parts last formed. Erb[42] has expressed the opinion, held now by many writers, that the most distant part of the neuron may be the first to degenerate. In K. K. the paresis was more evident in the lower limbs. Van Gehuchten's views possibly offer the best explanation for this condition, for the lumbar cord in K. K. seems possibly proportionally smaller than the cervical, as though many of the cervical fibres had not developed downward into the lumbar region.

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[35] Steinlechner-Gretschischnikoff: Archiv für Psychiatrie, vol. xvii., 1886.

[36] Ceni, quoted by Marinesco: Semaine Médicale, No. 48, 1896.

[37] Van Gehuchten: Journal de Neurologie, 1896.

[38] Starr: Journal of Nervous and Mental Disease, 1884, p. 343.

In examining some patients at the New Jersey Training School for Feeble-Minded Children, during the year 1896, the following cases seemed of sufficient importance in connection with this subject to be briefly described:

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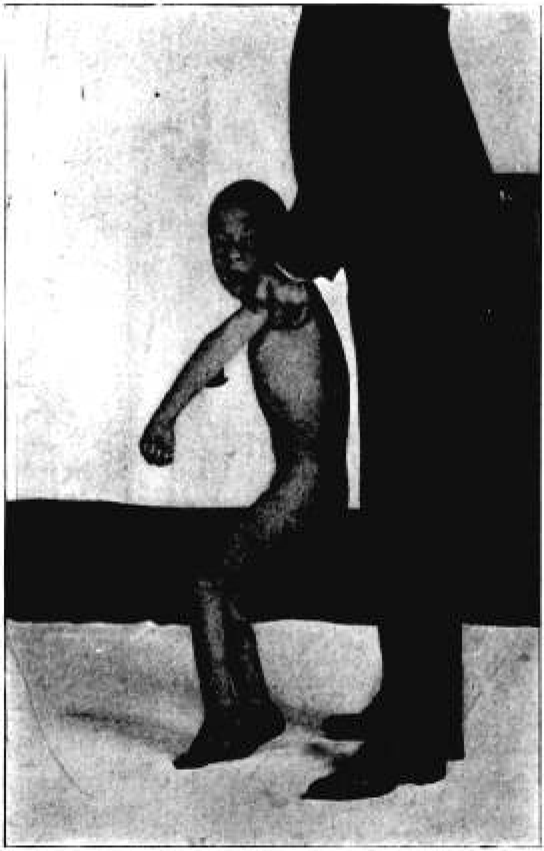
[39] Higier: Deutsche Zeitschrift für Nervenheilkunde, vol. ix., p. 31.

[40] Sachs: Volkmann's Sammlung klin. Vorträge, 46-47, 1892, p. 448.

[41] Strümpell: Archiv für Psychiatrie, vol. xvii.

[42] Erb: Deutsche Zeitschrift für Nervenheilkunde, vol. i., p. 240, and Neurologisches Centralblatt, 1883, p. 481.



A. S. (Little's disease).

The patient A. S. presents great similarity in his appearance to the case K. K., which has been examined microscopically. The circumference of the head measures 17 1-2 inches. His intellectual powers are very feeble, and he never speaks. The saliva dribbles constantly. The entire body is covered with a papular eruption. The hands and feet are always cold. He has no power of motion in the lower limbs, and makes no attempt to stand. When placed upon his feet he sinks at once to the ground. Both legs are much flexed at the knees, and cannot be extended by passive movement. The feet are in the position of talipes equinus, and can only be extended and flexed to a very slight degree by passive movement. The resistance in the thighs to passive movement is considerable. The patellar reflex is increased, but owing to the rigidity of the limbs the full degree of exaggeration is not perceptible. Ankle clonus and Achilles tendon reflex cannot be obtained on account of rigidity. In striking one patellar tendon slight adduction is observed of the opposite thigh (crossed reflex). The limbs and trunk are well nourished. The fingers are held flexed upon the thumb, but can be extended passively. The patient can very awkwardly pick up a large object with either hand. The reflexes of the upper limbs (at wrist, elbow, and biceps tendon), are exaggerated, but are partially checked by the muscular spasticity. The patient has some power of motion in the upper limbs. Strabismus is not present. As the boy understands a few simple commands, the sense of hearing cannot be destroyed. His vision apparently is good. The pupils are equal. He cannot sit alone, and unless supported he falls upon the bed. The child was born at the seventh month, in ordinary labor. As a baby he was strong, but "two years after birth he simply stopped developing, without any apparent cause." The mother was only seventeen when this child was born. One sister of the patient is living and healthy. It is stated in the history that the boy has said some words. He has never had epilepsy.. He was born May 23, 1887.

This is a case of Little's disease, and is due to the cause which certain neurologists consider the only one which should be recognized,i.e., premature birth, and could his nervous system be examined lesions similar to those in K. K. might be found.

There are undoubtedly cases of arrested cerebral development which assume a paraplegic type. Sachs gave the proof of this in 1891. I have found three feeble-minded children at the New Jersey Training School in whom the lower limbs were alone affected. One is selected as an example.

R. C., eight years old, is a paraparetic idiot. He has never spoken, does not understand what is said to him, and takes no notice of anything. The limbs and trunk are well nourished. He cannot walk, and makes no attempt to take a step. In the erect position he inclines backward, and has to be supported or would fall. He can move his legs when in the sitting posture. Knee-jerk and ankle-jerk are exaggerated, and slight ankle clonus is present. Above the hips the movements are good. The reflexes in the upper extremities are not notably exaggerated. Strabismus is not observed, and the pupils are equal. The head is well developed. This child was born at full term in easy labor. A few months after birth he had convulsions. As a babe he was said to be strong. His condition was congenital. Other children in the family are healthy.

Three or four months after the above description was written the patient died in status epilepticus, and fortunately a necropsy was obtained, and microscopic examination of brain and cord was made. Within a few days previous to death the patient was said to have had many convulsions. The body was much emaciated. The dura was somewhat adherent to the calvarium, and the pia, especially over the left parieto-occipital lobe, was congested. I am indebted to Dr. C. W. Burr for the material.

The brain, especially in the left hemisphere, presents a low type of fissuration. In the left hemisphere the parallel fissure unites with the Sylvian, the ascending frontal is almost fully united with the Sylvian, the first frontal is so distinct that it forms almost a straight line, and the Sylvian fissure extends almost to the upper border of the hemisphere.

In sections from the superior part of the right ascending frontal convolution, there is a diminution in the number of the pyramidal cells, and all are much smaller than the giant cells *(Riesenzellen)* of the normal cortex used for comparison. The nerve cells also present an appearance of imperfect development, though some are of fair size. In the paracentral lobule a few giant cells are present, but these cells are not nearly as numerous as in a normal cortex.

Within the cord all parts seem to stain equally well, and it is impossible to note any diminution in the number of the fibres in the crossed pyramidal tracts, and these tracts do not contain the many fine fibres observed in the case K. K. In this respect the contrast is striking. The cells of the cervical enlargement are numerous and well formed. In the lumbar region the motor cells are also large and abundant, and if there is diminution in the number of these it cannot be excessive.

How shall we explain the paraplegia? It is probable, as Ganghofner suggests in regard to his cases, that the fibres of the pyramidal tracts are really fewer in number, although the microscope is too poor an instrument to detect this. Everyone who has studied the nervous system will acknowledge that it is difficult, or even impossible, to detect a moderate decrease in the number of fibres in a given tract. The condition of the cortex justifies the opinion advanced. It is possible that proportionally more motor fibres in growing downward reached the cervical region than the lumbar.

There are other cases of undoubted arrested development in which the power of motion is not greatly affected. There is a picture of the following case in Mills' paper in Starr's[43] book on the diseases of children.

J. M. is a microcephalic idiot of low grade, and not taller than a child of four or five years. He was born January 31st, 1870. The circumference of the head is 16 1-4 inches. He can talk, but his words convey no meaning. He has epilepsy, and may have as many as two or three attacks in a night, though on an average he has two or three in a week. He is very bow-legged, and this condition is evidently due to rachitis. He scratches and bites, and it is impossible to attract his attention. He does not understand anything said to him. He can walk, usually slowly, although he can be made to run. The right foot is planted firmly on the ground, but the left is kept elevated. His gait is not spastic. He moves the upper extremities freely, but slowly. The color of the irides is different; in one eye it is gray, in the other hazel. The right pupil is slightly larger than the left, and is irregular. Movement of the eyeballs is free. Sensation for pain is well preserved. The knee-jerk and ankle-jerk are exaggerated, and there is slight ankle clonus. Strabismus is not present. The reflexes in the upper extremities at the wrist, olecranon, and biceps tendon are exaggerated on both sides, but not so much as those in the lower extremities. One might be surprised to find motion in the extremities so good in a case of microcephaly of high grade, but paralysis is in no way due to small size of the head. Puberty has been attained. It is difficult to test the reaction of the pupils to light and accommodation, as it is impossible to make the man (?) keep his eyes open and fix an object. He was the third in the family, and was born at full term in normal labor. The father kept a saloon, and was inclined to indulge in alcoholic beverages. The patient had four sisters living and healthy in 1888. Six children have died from infectious diseases, and one from marasmus. There were no other malformed children.

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[43] An American Text-Book of the Diseases of Children. Edited by Louis Starr, M.D.

After this paper was written my attention was called by Dr. Adolf Meyer, of the Worcester Lunatic Hospital, to the work of Hammarberg[44] which is of so great importance that a brief abstract must be given. The chief aim of this paper has been the investigation of the causes of paresis and paralysis in cases of idiocy and microcephaly, and considerable evidence of the important part the giant cells *(Riesenzellen)* of the motor cortex have in the function of motion has been obtained. Hammarberg's work is confirmative of this view, and the abstract relates chiefly to his investigations on the ascending frontal gyrus. The results of his examination of the cerebral cortex must be read in the original. No abstract can do justice to a work of this magnitude.

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[44] Carl Hammarberg: Studien über Klinik und Pathologie der Idiotie, etc.

While the chief aim of this paper has been the investigation of the causes of paralysis, the causes of imbecility have also in part been mentioned, for it must follow, that if the cortical zones which form the projection centres are arrested in their development during the embryologic period, or even the first month of extrauterine life, that this arrest will cause a corresponding arrest in the development of the association centres, as an inevitable consequence, and in this way an arrest in the development of the intellectual faculties (Flechsig, as quoted by Van Gehuchten.)[45]

The giant-cells (Hammarberg) measure 35-40x50x80 microns in the anterior central gyrus. These have been called "ganglionic cells" by Bevan Lewis and Clarke.

Under the title of *Blödsinnige* (dements) four cases are reported by Hammarberg. The first child was twenty-two months old. During the first year of life it made no spontaneous movements. In the medial and upper half of the lateral aspect of the anterior central gyrus, as well as in the adjoining part of the frontal convolutions, the cells were arranged in one layer. They resembled the undeveloped cells of a fetus of five months, although they were larger than these, and yet smaller than normal cells, and they represented about one-fifth the normal number. A few undeveloped spindle cells were noticed.

Case 2. 14 years old. The child could not walk or sit erect, and there was paresis in the upper, and paralysis in the lower extremities. The anterior central gyrus.

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[45] Van Gehuchten: Journal de Neurologie, January 5, 1897.

the posterior half of the lateral aspect of the inferior frontal gyrus, and the superior and inferior parietal gyri were the least developed. The cells were arranged in a single layer, and resembled embryonal cells, and were smaller than in normal persons of the same age.

Case 3. 10 years old. The cells in the anterior central gyrus were somewhat smaller and fewer than in normal brains. Groups of giant cells in normal number were observed. This case differed from the other two in that mobility was greater.

Case 4. 3 years old. The child could sit alone and walk, very insecurely, on level ground. In the right anterior central gyrus the pyramidal cells did not amount to one-fifth the usual number, and they were mingled with undeveloped cells. There were also cells which presented a hyaline appearance. In the lower part of the gyrus more large cells were noticed.

The larger part of the cerebral cortex in these four cases represented the normal degree of development in the latter half of fetal life. The different clinical symptoms could be explained by the cortical findings.

Two feeble-minded children of low grade are described:

Case 5. 26 years old. Movements were slow, but the patient could walk, although was soon exhausted. In the anterior central gyrus the cells and layers were somewhat smaller than in a normal person of the same age. The giant cells measured 25-30x50 microns. The slow movements could not be explained by the findings in the motor region. Possibly the decrease in the cells of the vermis was connected with the slow movements.

Case 6. 1 year, 10 months old. The child could not walk or sit erect. The imperfect mobility was not only due to the undeveloped condition of the cortex in the motor region, as this corresponded merely to the degree of development seen at the end of the first year, but also to the fact that the cells, and especially the giant cells, were much fewer than normal.

In these two cases the greater part of the cerebral cortex corresponded to the degree of normal development in the first years of life.

Three cases of moderate and slight grades of mental development are described:

Case 7. 14 years old. There was complete paralysis of the lower extremities and paresis of the upper. This was explained by the fact that the corresponding parts of the motor cortex were not more developed than in the first year of normal life, and the giant cells in the upper part of the anterior central gyrus were absent. In the lower parts of the gyrus the cells were larger and the appearance more like the normal.

Case 8. 12 years old. Mobility was not impaired. In the anterior central gyrus the cells were normal, although fewer. The giant cells were relatively most numerous.

Case 9. 16 years old. Both lower extremities were paretic, and the patient could not stand. The movements in the upper limbs and trunk were normal. The medial and upper sixth of the lateral aspect of the anterior central gyrus, the posterior central gyrus, and the inferior frontal gyrus were most altered, and the cells presented an undeveloped appearance. In the rest of the cortex the cells were normal, but fewer than in normal brains. There were no giant cells in the upper part of the anterior central gyrus.

In these three cases the number of the nerve cells in the greater part of the cerebral cortex was much less than the normal, and in a small area they represented the degree of development in the first years of life.

From the results of these important examinations Hammarberg concluded that the mental condition depends on the degree of development of the brain as represented by the cortical cells.

Surely in view of the testimony which has been presented by macroscopical and microscopical examination of the central nervous system in cases of microcephaly, one must acknowledge that the operation of craniotomy is one which deserves most careful consideration. Perls and Edinger[46] have shown that hydrocephalus of mild degree occurring in childhood and not progressing, or rachitis involving the skull, have seemed to favor the mental development by lessening the resistance to the growth of the brain, but in these cases nerve cells were already present. It may be, as Starr[47] suggests, that operation stimulates the growth of cerebral tissue, but probably it can never cause the production of new nerve cells. We can never be perfectly sure of the nature of the lesion in any case of microcephaly. Dr. Keen has most kindly consented to give his views on the advisability of the operation of craniotomy in microcephaly, and the results obtained from his experience of many years are of inestimable value. I thank him most heartily for this important addition to my paper.[48]

REMARKS BY W. W. KEEN, M.D., ON THE ADVISABILITY OF OPERATION IN MICROCEPHALY.

I am glad that Dr. Spiller has been so fortunate as to be able to make a very careful post-mortem examination of the little girl K. K. reported in this paper. I cheerfully consent, at his request, to give my views on the present status of the operation of linear craniotomy.

My views are based not only on what I have learned from the experience of others, but upon a personal experience covering eighteen cases. Of these eighteen cases five died, a mortality of 21.7 per cent. The youngest was eighteen months old, the oldest six and a half years. As to their later history I can report of the thirteen who recovered that six were slightly improved, seven were not benefited.

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[46] Edinger: Vorlesungen über den Bau der nervösen Centralorgane. Fifth edition.

[47] Starr: Medical Record, 1892, vol. i.

[48] Since this paper was written important works bearing on the subject of microcephaly and idiocy have been published by Pfleger and Pilcz (Arbeiten aus dem Institut für Anatomie und Physiologie. Obersteiner, No. v.) and by Kaes (Monatsschrift für Psychiatrie und Neurologie, No. i., 1897.)

On the whole the prospect for improvement after the operation of linear craniotomy for microcephalus is not bright. Sometime since a patient called upon me who had sought advice as to her child, and when I told her that nothing could be done, the boy being simply an idiot with an average sized head and not the slightest indication favorable to operation, she was astonished to the last degree, and more than that she was heart-broken. She had been encouraged to believe that even in hundreds of operations not a death had taken place, and she stated that the very words used to her were that if she would allow an operation to be done "the result would be a revelation to her." Two specific instances of great improvement were cited to her. When I investigated these two cases I found that both were again in an asylum in a worse condition than before the operation. One can imagine what a crushing blow it was for a fond mother, who had anticipated a speedy cure for her idiot boy and a restoration to a normal intellectual life, to be told that such statements were not borne out by facts, and that in my opinion absolutely no good could result from operation.

I do not consider that a child with an average sized head is a suitable case for operation, nor secondly that in cases older, we will say, than about seven years of age, improvement can be expected. Nor do I regard the operation justifiable in those suffering from extreme microcephaly in which the head is *excessively* small. Only the cases showing a moderate degree of microcephaly are suitable for operation. The cases with *very* small heads, as the child K. K. reported in this paper by Dr. Spiller, as he has shown, have a very imperfect development of the nerve cells, which are essential for a normal or even approaching a normal life. In less extreme cases where probably the cells are more perfect we may hope for more. As I have said elsewhere (Medical News, November 29th, 1890, p. 558) "The inherent cause of microcephalus we do not know. Formerly it was supposed to be due to premature ossification of the cranial sutures, but the examination of several such skulls has shown that while this may sometimes be the case, yet in the cases examined there was no abnormality in the bony development of the cranium. On the other hand, we know that the growth of the skull keeps pace with the growth of the brain within it; and if the growing power of the brain be weak, a slight resistance on the part of its osseous envelope may be sufficient to check and stunt it."

The benefit so far as my observation goes is but slight. When the American Surgical Association met in Buffalo about three years ago, Dr. Roswell Park showed a boy, I think about twelve years of age, who had been very greatly benefited by the operation, so that he had, one might say, three-quarters of a normal intellectual development. I have never seen in any of my own cases any such improvement, and this case surprised me the more in view of the boy's age, which I think was about ten when he was operated on. Any real improvement, however, would justify the operation in my opinion. One of my cases for instance, was the child of a poor washer-woman with several other children. He was as restless, and as mischievous as a monkey. At night he was almost constantly crying, and so disturbed his mother that she had scarcely had one good night's rest since he was born. The operation transformed him into a quiet, fairly sleepful child, and was well worth any risk which attended the operation.

In fact, if any one may speak of risk, we can honestly only wish that in all the cases which should not be benefited the risk would be far greater than it is, since if such children cannot be helped it is far better for them, their parents and other caretakers and their companions that they should die.

I suppose I have declined to operate on at least one hundred cases which in my opinion were entirely unsuitable for operation.

My present conclusions, therefore, are:

(1) That in a moderate number of selected cases of medium degrees of microcephaly the operation will happily be followed by death in about fifteen to twenty per cent. of the patients.

(2) In a small number of cases benefit to a slight extent will be observed, but in the majority no results, good or bad, will follow the operation.

Were we to judge from the microscopic results in the case Dr. Spiller has so ably investigated, we should unquestionably say that no good result could ever follow, but we must remember that this child had an extremely small head, and was a case in which, with a now larger experience, I should absolutely decline to operate, and also, that this child did actually improve to some extent, whether as the result of the operation, or of the later excellent training and care that she had, we cannot judge positively. Clinically there is no question about a moderate improvement in a small number of cases.

After operation the greatest attention should be paid to developing the child's faculties by education. This can hardly be done in, or by any family. It is best done in a school such as that of the Misses Bancroft and Cox in Haddonfield, N. J., where a long familiarity with such cases enables them to adopt means to ends, to develop better methods of education which result from a wide experience, and to provide an individual teaching which neither in a family nor in a large school is practicable. How much improvement comes from the education and how much from the operation is often a matter of great uncertainty.

In all cases a clear statement of the mortality should be made to the parents and they should be prepared for a very probable disappointment in seeing only very slight good results or none at all, and then they must decide whether they are willing to accept the risk of death and the risk of disappointment.